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1: Infect Immun. 2001 Feb; 69(2): 1025-31.

Cure of Helicobacter pylori infection and resolution of gastritis by adoptive transfer of splenocytes in mice.

Eaton KA, Mefford ME.

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Vaccination suppresses Helicobacter pylori colonization but does not cure infection. Furthermore, postvaccination gastritis, likely induced by enhanced host response to residual colonization, may exacerbate disease. The goal of this study was to determine if adoptive transfer of C57BL/6 splenocytes to C57BL/6scid/scid (severe combined immunodeficient [SCID]) mice cures infection without exacerbating gastritis. H. pylori-infected and uninfected C57BL/6 mice and SCID recipients of normal splenocytes were killed at intervals between 5 and 51 weeks after infection. Colonization and gastritis were quantified, humoral immune responses were determined by enzyme-linked immunosorbent assay, and cellular immune responses were determine by delayed-type hypersensitivity response and by a proliferative response of cultured splenocytes to H. pylori sonicate. In infected C57BL/6 mice, gastriti developed gradually and bacterial colonization diminished but persisted throughout the experiment. In contrast, gastritis in infected recipient SCID mice developed rapidly and bacterial colonization decreased precipitously. Gastritis in those mice peaked 9 weeks after adoptive transfer, however, and began to resolve. By 45 weeks after transfer, gastritis had returned to background levels and bacteria were no longer detectable. Resolution of gastritis and elimination of infection were associated with a cellular but not humoral immune response to H. pylori antigens. These results demonstrate that although the host response fails to clear bacterial colonization in normal mice, enhanced cellular immune responses in recipient SCID mice are capab of clearing H. pylori infection and allowing resolution of gastritis. Thus, immune mechanisms of cure exist, and effective and safe vaccination protocols may be feasible.

PMID: 11159999 [PubMed - indexed for MEDLINE]

1: Proc Natl Acad Sci U S A. 2000 Jul 18; 97(15): 8473-8. Related Articles, Lin

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Comparative T cell receptor repertoire selection by antigen afte adoptive transfer: a glimpse at an antigen-specific preimmune repertoire.

Attuil V, Bucher P, Rossi M, Mutin M, Maryanski JL.

Institut National de la Sante et de la Recherche Medicale, Unit 503, Ecole Normale Superieure de Lyon, 69007 Lyon, France.

The low frequency of precursor cells specific for any particular antigen (Ag) makes it difficult to characterize preimmune T cell receptor (TCR) repertoire and to understand repertoire selection during an immune response. We have undertaken a combined adoptive transfer single-cell PCR approach to probe the Ag-specific preimmune repertoires of individual mice. Our strategy was t inject paired irradiated recipient mice with normal spleen cells prepared from individual donors and to compare the TCR repertoires subsequently selected during a CD8 response to a defined model Ag. We found that although some TCRs were shared, the TCR repertoires selected by mice receiving splenocytes from the same donor were not identical in terms of the TCRs selected and their relative frequencies. Our results together with computer simulations imply that individual mice express distinct Ag-specific preimmune TCR repertoires composed of expanded clones and that selection by Ag is a random process.

PMID: 10900008 [PubMed - indexed for MEDLINE]

1: Eur J Immunol. 2000 May; 30(5): 1297-307.

Tumor size at the time of adoptive transfer determines whether tumor rejection occurs.

Cordaro TA, de Visser KE, Tirion FH, Graus YM, Haanen JB, Kioussis D, Kruisbeek AM.

Division of Immunology, The Netherlands Cancer Institute, Amsterdam, The Netherlands.

Here we investigate the minimal requirements for induction of an anti-tumor response in CD8 T cells in vivo. We compare the efficacy of adoptive transfe of CD8 T cells with a transgenic TCR specific for the main cytotoxic T lymphocyte epitope of the influenza virus nucleoprotein (NP) on the growth NP-expressing EL4 tumors under different conditions. In a setting in which tumor rejection is solely dependent on tumor-specific CD8 T cells, small immunogenic tumors fail to induce a rejection response, despite the fact that they are not ignored: tumor-specific CD8 T cells are activated, differentiate into effector cells and infiltrate the tumor bed. Nevertheless, tumor rejection does not occur. In sharp contrast, the same immunogenic tumor, when growing as a large tumor mass, is rejected by transferred tumor-specific CD8 T cells. The main features which distinguish the rejection response to a large tumor mass from the response to a small tumor is that, in the latter case, activated CD8 T cells appear much later, and in much smaller numbers. Efficacy of adoptive transfer is thus dictated by the size of the tumor mass at the time of transfer. These findings predict that treatment of minimal residua disease with adoptive transfer will fail, unless vaccination is also provided at the time of transfer.

PMID: 10820375 [PubMed - indexed for MEDLINE]

1: Hum Gene Ther. 1993 Oct; 4(5): 659-80.

A study of the safety and survival of the adoptive transfer of genetically marked syngeneic lymphocytes in HIV-infected identical twins.

Walker R, Blaese RM, Carter CS, Chang L, Klein H, Lane HC, Leitman SF, Mullen CA, Larson M.

This phase I/II pilot project will evaluate the survival, tolerance, safety, and efficacy of infusions of activated, gene marked, syngeneic T lymphocytes obtained from HIV seronegative identical twins on the functional immune status of HIV infected twin recipients. T cells from each seronegative twin will be obtained by periodic apheresis, separated into CD4 and CD8 enriched populations by monoclonal antibody affinity binding techniques, induced to polyclonal proliferation with anti-CD3 and rIL-2 stimulation, transduced with distinctive neoR retroviral vectors, and expanded 10-1,000 fold in numbers during approximately 2 weeks of culture. These marked T cell fractions will then be infused into the seropositive twins and the survival of the uniquely marked T cell populations will be monitored by vector-specific PCR, while the recipients' functional immune status is monitored by standard in vitro and in vivo testing protocols. A total of 3 cycles of treatment will be given at intervals of 6 weeks between infusions.

Publication Types:
- Clinical Trial
- Clinical Trial, Phase I
- Clinical Trial, Phase II

PMID: 8280803 [PubMed - indexed for MEDLINE]

1: Clin Diagn Lab Immunol. 1997 Sep; 4(5): 630-2.

Antibodies to the hepatitis B e antigen (HBeAg) can be induced in HBeAg-transgenic mice by adoptive transfer of a specific T-helper 2 cell clone.

Hultgren C, Milich DR, Sallberg M.

Division of Clinical Virology, Huddinge University Hospital, Sweden.

Production of antibody to hepatitis B e antigen (HBeAg); i.e., anti-HBe antibody,) in HBeAg-transgenic mice is believed to be mediated by T-helper (Th2) cells. Injection of an HBeAg-specific Th2 clone into HBeAg-transgeni H-2k mice induced anti-HBe antibody production, confirming the function o Th2 cells in this model system.

PMID: 9302220 [PubMed - indexed for MEDLINE]

1: Scand J Immunol. 1996 Mar; 43(3): 283-8. Related Articles, Lin

Cancer prevention by adoptive transfer of antigen 60-activated immunocompetent cells.

Maes H, Cocito C.

Laboratory of Microbiology and Molecular Genetics, Medical School, University of Louvain, Brussels, Belgium.

The authors have already shown that A60, the thermostable macromolecular antigen complex of Mycobacterium bovis BCG, induced resistance to tumou challenge in several murine systems. In the present work, the authors provide evidence that activated macrophages played a major role, and cytolytic T lymphocytes a minor one, in both in vivo and in vitro A60-promoted cancer cell cytolysis. To identify the types of immunocompetent cells involved in th protective effect, macrophages and T lymphocytes from A60-primed mice donors were adoptively transferred to irradiated recipients prior to EMT 6 tumour challenge. In some groups, A60-primed donors were survivors of previous tumour challenges. Transfer of T lymphocytes from the spleen or lymph-nodes of A60-immunized mice induced 80-90% protection against tumour challenge. Conversely, transferred macrophages, although cytolytically active, did not induce resistance to tumour implantation. Furthermore, adoptive transfer with T lymphocytes from A60-immunized an EMT 6 challenge-surviving donors induced 100% protection. It is concluded that stimulation of T lymphocytes by A60 is the key step which leads to activation of the immunocompetent cells involved in tumour rejection.

PMID: 8602462 [PubMed - indexed for MEDLINE]

1: J Autoimmun. 1994 Dec; 7(6): 819-31. Related Articles, Lin

ELSEVIER

Adoptive transfer of autoimmune diabetes mellitus to athymic rats: synergy of CD4+ and CD8+ T cells and prevention by RT6 T cells.

Whalen BJ, Greiner DL, Mordes JP, Rossini AA.

Department of Medicine, University of Massachusetts Medical School, Worcester 01655.

We describe the induction and prevention of autoimmune insulin dependent diabetes mellitus (IDDM), and its pathological substrate, insulitis, in congenitally athymic nude rats following injections of major histocompatibility complex (MHC) compatible lymph node T cells. The cells capable of adoptive transfer of autoimmunity were obtained from diabetes resistant (DR) BB rats that had been rendered hyperglycemic by in vivo depletion of the RT6+ regulatory T cell subset. We first established that our adoptive transfer assay system is cell dose- and time dependent and therefore amenable to quantitative analysis. It was also observed that both CD4+ and CD8+ T cells are required for efficient transfer of autoimmunity. The data indicate that, as in the NOD mouse, a synergistic interaction between CD4+ and CD8+ T cells is important for beta cell destruction. Finally, we demonstrated that the admixture of equal numbers of lymph node T cells, 60' of which were RT6+, from intact, non-diabetic DR rats prevented the adoptiv transfer of IDDM mediated by diabetogenic T cells from RT6-depleted DR-BB rats. We conclude that an equilibrium between autoreactive and regulatoi cells determines the expression of autoimmunity in the DR-BB rat and in the adoptive transfer of diabetes in quantitative analytical systems.

PMID: 7888038 [PubMed - indexed for MEDLINE]

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1: Immunology. 1992 Apr; 75(4): 693-9. Related Articles, Lin

Adoptive transfer of the generalized lymphoproliferative disease (gld) syndrome in nude beige mice.

Froidevaux S, Rosenblatt N, Loor F.

Laboratoire d'immunologie, Universite Louis Pasteur, Strasbourg, France.

C57BL/6 nude beige mice (B6 nubg) were used as recipients for the transfer of haematopoietic cells from either B6 wild as control mice, or systemic lupu erythematous B6 mice homozygous for the recessive generalized lymphadenopathy disease (gld) locus. Both gld and wild cell grafts prolonge survival of the short-living B6 nubg recipients and restored some T-cell functions, as monitored by the presence of T-dependent Ig isotypes in the serum and responsiveness of spleen cells to a T-cell mitogen. Moreover, the [gld----nubg] chimeras but not the [wild----nubg] chimeras showed several similarities with gld control mice, particularly, a spleen and lymph node hyperplasia, elevated anti-single-stranded DNA antibody titres and a hyperglobulinaemia. This hyperglobulinaemia was however qualitatively different from the gld-type hyperglobulinaemia with an important contributic of the IgG1 isotype; the lymph node hyperplasia was also less marked than i B6 gld mice.

PMID: 1592442 [PubMed - indexed for MEDLINE]

1: Adv Immunol. 1991; 50: 303-25.

Adoptive transfer of human lymphoid cells to severely immunodeficient mice: models for normal human immune function, autoimmunity, lymphomagenesis, and AIDS.

Mosier DE.

Division of Immunology, Medical Biology Institute, La Jolla, California 92037.

Though the development of human-to-mouse xenotransplant models is in its infancy, astonishing progress has been made in a short period of time. Two experimental applications have been developed: short-term transfer of humar lymphocytes to generate models for autoimmunity and infectious diseases, and long-term engraftment of tissues with self-renewal potential. Human PBL-SCID mice have been used by multiple laboratories to study normal anc autoimmune antibody responses, and have been shown to be readily infectab with HIV-1. SCID mice grafted with fetal tissue have been developed for studies of HIV-1 infection and its therapy as well as for studies of human hematopoietic cell differentiation. Human tumors appear to grow better in SCID mice than in nude mice, and hu-PBL-SCID mice can develop EBV-related B cell lymphoproliferative disease that resembles the immunoblastic lymphomas appearing in immunosuppressed transplant recipients. There is some evidence of mouse NK cells responding to the human xenograft, and of human T and B cells responding to mouse xenoantigens in these models, but these responses are not generally strong enough to have a major impact on human immune function. The use of these surrogate human models is expected to have a major impact on the understanding and treatment of huma disease.

Publication Types:
- Review
- Review, Tutorial

PMID: 1950798 [PubMed - indexed for MEDLINE]

1: Proc Natl Acad Sci U S A. 1990 Oct; 87(19): 7618-22. Related Articles, Lin

Adoptive transfer of autoimmune diabetes and thyroiditis to athymic rats.

McKeever U, Mordes JP, Greiner DL, Appel MC, Rozing J, Handler ES Rossini AA.

Department of Medicine, University of Massachusetts Medical School, Worcester 01655.

We describe the induction of autoimmune diabetes, insulitis, and thyroiditis i athymic rats following injections of major histocompatibility complex compatible spleen cells. Lymphocytes with these capabilities were found in normal rats of the YOS, WAG, PVG, and diabetes-resistant BB strains, and i diabetes-prone BB rats. Adoptive transfer was facilitated by prior in vivo depletion of RT6.1+ regulatory T cells and in vitro mitogen activation of donor spleen cells. By RT6 depleting diabetes-resistant donors and using nuc recipients, transfer of diabetes and thyroiditis was accomplished by using fresh, unstimulated spleen cells. The data suggest that organ-specific autoreactive cells may be present to various degrees but suppressed to a variable extent in many rat strains. The equilibrium between autoreactive anc regulatory cells appears to determine the expression of autoimmunity.

PMID: 2217193 [PubMed - indexed for MEDLINE]

1: Cancer Res. 1990 Dec 1; 50(23): 7450-6.

Adoptive transfer of tumor cytotoxic macrophages generated in vitro from circulating blood monocytes: a new approach to cancer immunotherapy.

Andreesen R, Scheibenbogen C, Brugger W, Krause S, Meerpohl HG, Leser HG, Engler H, Lohr GW.

Medizinische Klink I, Albert-Ludwigs-Universitat Freiburg im Breisgau, We Germany.

Cells of the macrophage lineage are considered to be of special importance i the defense of the host against tumor development and spread. Immunotherapeutic strategies to stimulate macrophage (MAC) tumor cytotoxicity make use of activating compounds such as gamma-interferon which are given systemically. However, there are several lines of evidence that in malignant disease the generation of cytotoxic effector MACs is impaired. Both defective cell maturation and loss of responsiveness to activation are described. Here, a first clinical phase I trial of adoptive immunotherapy in cancer patients using autologous MACs generated in vitro from blood monocytes (MOs) is reported. Mononuclear cells were isolated b cytapheresis and density centrifugation and cultured in hydrophobic Teflon bags for 7 days with 2% autologous serum and recombinant human gamma-interferon being present for the last 18 h. Cytotoxic MO-derived MACs were then purified by countercurrent elutriation and reinfused into the patient. A total of 72 therapies have been performed with patients being treated i.v. (n = 8) and i.p. (n = 7). In vitro generated MACs proved to be mature as judged b the expression of maturation-associated surface molecules (MAX antigens, CD16, CD51, CD71), were cytotoxic to U937 tumor cells, and were efficient secretory cells. Cell dose escalation was performed in the first patients beginning with 10(8) MACs to finally infuse the total number of cells recovered from one single cycle of isolation and culture. MAC yield varied from 1 to 17 x 10(8) representing 13-79% of MOs initially seeded. Adoptive MAc transfer was well tolerated. Side effects observed were low-grade fever (less than 38.5 degrees C), induction of the coagulation cascade, and abdominal discomfort after i.p. application. The procoagulant activity of MA autografts was cell dose dependent and demonstrated by detection of circulating fibrin monomers and thrombin-antithrombin complexes. Biological responses observed included elevated serum neopterin levels and

the appearance of interleukin-6 in sera and ascitic fluids. Indication of a possible therapeutic effect was only observed in i.p.-treated patients and consisted of disappearance of malignant ascites in 2 of 7 patients.

Publication Types:
- Clinical Trial

PMID: 1701343 [PubMed - indexed for MEDLINE]

1: J Immunol. 1983 Mar; 130(3): 1478-82.

Adoptive transfer of resistance to growth of an idiotype-secretin hybridoma by T cells from idiotypically suppressed mice.

Kresina TF, Baine Y, Nisonoff A.

A/J or CAF1 mice that are suppressed with respect to an idiotype, CRIA, associated with anti-Ar antibodies, and hyperimmunized develop high concentrations of idiotype-suppressor T cells. In this paper we show that sucl CAF1 mice are resistant to the growth of a CRIA-positive hybridoma that is lethal in normal or in immunized non-suppressed mice. No resistance was observed to the growth of a hybridoma secreting anti-Ar antibodies that lack CRIA. The state of resistance could be adoptively transferred to naive syngeneic recipients with spleen cells or T-enriched spleen cells from suppressed hyper-immunized mice; B-enriched cells were ineffective.

PMID: 6600485 [PubMed - indexed for MEDLINE]

1: J Gen Virol. 1981 Sep; 56(Pt 1): 25-31.

Recovery from experimental rabies by adoptive transfer of immune cells.

Prabhakar BS, Fischman HR, Nathanson N.

The transient, sublethal infection produced by intracerebral inoculation of the Flury high egg passage (HEP) strain of rabies virus into adult mice was converted into a lethal one (approx. 80 to 100% mortality) by administering 150 mg/kg cyclophosphamide (CY) 2 days after infection. Immunosuppressed, infected animals showed no immunological response to rabies and died 15 to 20 days after infection. However, mortality was reduced to 12% when suppressed mice were adoptively immunized, 4 days after infection, with an intravenous injection of 60 X 10(6) spleen cells from rabie immune syngeneic donors. The lymphocytes obtained early after donor immunization (4 to 11 days) reduced mortality, whereas those obtained late (16 to 32 days after immunization) were not effective. The ability of donor cells to protect animals corresponded very closely with donor cytotoxic T lymphocyte (CTL) activity. Within 4 days after immune cell transfer, serum neutralizing antibody and CTL levels in recipients were comparable to those found in virus-infected control animals. Immune donor cells were fractionate into thymus-derived (T-enriched) and bone marrow-derived (B-enriched) subsets. The T and B subsets reduced mortality to 32% and 34% respectively CTL and serum neutralizing antibody responses could be detected in these animals, although they appeared later than in mice treated with unfractionate immune spleen cells. The present study demonstrates that both B and T lymphocytes are required for optimum clearance of rabies from the central nervous system (CNS) and suggests a functional role for rabies-specific CTL in vivo.

PMID: 6975354 [PubMed - indexed for MEDLINE]